

CLAIMS

What Is Claimed Is:

1. A combinatorial library of indolinone
compounds, comprising a series of at least ten indolinones
5 that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein
said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein
said aldehydes are type B aldehydes.

10 4. The combinatorial library of claim 1 wherein
said library comprises at least 100 indolinones.

5. The combinatorial library of claim 1 wherein
said library comprises at least 1000 indolinones.

15 6. The combinatorial library of claim 1,
wherein most of said indolinones are in the cis
conformation.

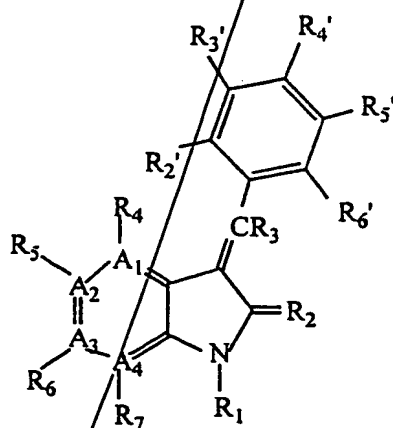
7. A method of making an indolinone comprising
the steps of

(a) creating a combinatorial library of

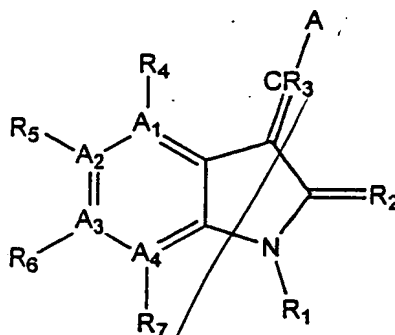
indolinones by reacting a series of
oxindoles with a series of aldehydes,

- (b) testing said indolinones in biological assays,
(c) selecting one or more indolinones with favorable
activity; and
(d) synthesizing one or more of said indolinones
selected in step (c).

8. A compound having formula V or VI



(V)



(VI)

Figure 6

Figure 6 displays six histograms showing the distribution of the number of nodes per cluster (n_c) for different values of α . The x-axis represents the number of nodes per cluster (n_c), ranging from 0 to 10. The y-axis represents the frequency or probability density, ranging from 0 to 0.08. The distributions are labeled as follows:

- (a) $\alpha = 0.0$: Shows a highly concentrated distribution at $n_c = 1$.
- (b) $\alpha = 0.1$: Shows a slightly broader distribution centered around $n_c = 1$.
- (c) $\alpha = 0.2$: Shows a more spread-out distribution with a peak around $n_c = 1$.
- (d) $\alpha = 0.3$: Shows a distribution shifted towards larger n_c , peaking around $n_c = 2$.
- (e) $\alpha = 0.4$: Shows a distribution shifted further towards larger n_c , peaking around $n_c = 3$.
- (f) $\alpha = 0.5$: Shows a distribution shifted significantly towards larger n_c , peaking around $n_c = 4$.

The histograms illustrate how the parameter α influences the clustering behavior, with higher values of α leading to clusters containing more nodes.

- (a) A_1 , A_2 , A_3 , and A_4 are independently carbon or nitrogen;
- (b) R_1 is hydrogen or alkyl;
- (c) R_2 is oxygen or sulfur;
- (d) R_3 is hydrogen;
- (e) R_4 , R_5 , R_6 , and R_7 are optionally present and are each independently selected from (i) the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, $S(O)R$, SO_2NRR' , SO_3R , SR , NO_2 , NRR' , OH , CN , $C(O)R$, $OC(O)R$, $NHC(O)R$, $(CH_2)_nCO_2R$, and $CONRR'$ or (ii) any two adjacent R_4 , R_5 , R_6 , and R_7 taken together form a fused ring with the aryl portion of the oxindole-based portion of the indolinone;
- (f) R_2' , R_3' , R_4' , R_5' , and R_6' are each independently

selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R, SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R, and CONRR';

- 5 (g) n is 0, 1, 2, or 3;
(h) R is H, alkyl or aryl; and
(i) R' is H, alkyl or aryl.
(j) A is a five membered heteroaryl ring selected from
the group consisting of thiophene, pyrrole, pyrazole,
imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, .
isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole,
1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole,
1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-
thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-
15 thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole,
and tetrazole, optionally substituted at one or more
positions with alkyl, alkoxy, aryl, aryloxy, alkaryl,
alkaryloxy, halogen, trihalomethyl, S(O)R, SO₂NRR', SO₃R,
SR, NO₂, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH₂)_nCO₂R or
20 CONRR'.

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound according to Claim 8.

10. A method for treating diseases related to
25 unregulated tyrosine kinase signal transduction, the method

11. A method for regulating tyrosine kinase signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.

EFFECT OF